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The Honorable Richard G. Andrews
United States District Court
for the District of Delaware
844 N. King Street
Wilmington, DE 19801

VIA ELECTRONIC FILING

Re: *United Therapeutics Corp. v. Liquidia Techs., Inc.*, C.A. No. 23-975-RGA

Dear Judge Andrews:

We write in response to the Court's request for comment on "whether the discussion of 'clinically proven effective' in *Bayer Pharma v. Mylan*, No. 23-2434 (Fed. Cir. Sept. 23, 2025) has any impact on whether the limitations added by dependent claims 5, 6, 9, and 17 of the '327 patent are entitled to any patentable weight in the anticipation/obviousness analysis of those claims." D.I. 455.

Bayer further confirms that these claims are entitled to patentable weight. The dependent claims of the '327 patent are nothing like the independent claim limitation found problematic in *Bayer*. Instead, the dependent claim limitations at issue here are like those upheld in *Allergan*, which the *Bayer* court expressly distinguished. *Bayer*, 2025 WL 2698408, at *3. Moreover, any argument Liquidia may make that these claims lack patentable weight is forfeited. UTC respectfully requests that—consistent with *Bayer*—this Court determine that claims 5, 6, 9, and 17 of the '327 patent are entitled to patentable weight for purposes of obviousness and anticipation.

I. The *Bayer* decision addressed a hollow limitation in an independent claim.

In *Bayer*, the Federal Circuit considered the phrase "clinically proven effective" in an independent method claim reciting administration of specific doses of two drugs to reduce cardiovascular risks. *Bayer*, 2025 WL 2698408, at *1. Claim 1 from *Bayer* is reproduced below with the dosing limitations highlighted in yellow:

> **1.** A method of reducing the risk of myocardial infarction, stroke or cardiovascular death in a human patient with coronary artery disease and/or peripheral artery disease, comprising administering to the human patient rivaroxaban and aspirin in amounts that are ***clinically proven effective*** in reducing the risk of myocardial infarction, stroke or cardiovascular death in a human patient with coronary artery disease and/or peripheral arterial disease, wherein rivaroxaban is administered in an amount of 2.5 mg twice daily and aspirin is administered in an amount of 75-100 mg daily.

Id. at *1 (emphasis added). In this claim, the term "clinically proven effective" describes the "amounts" of drugs that must be administered. However, the *Bayer* court found that this was synonymous with the specific 2.5 mg and 75-100 mg dosage amounts recited later in the claim. *Id.* The court therefore determined that the "clinically proven effective" term "cannot make the challenged claims patentable," "even if the phrase were limiting," because "[e]ven if the term required clinical proof of efficacy, such proof 'in no way transforms the process of taking the drugs' at the amounts and frequencies expressly recited in the claims." *Id.* at *2 (quoting *King Pharms., Inc. v. Eon Labs, Inc.*, 616 F.3d 1267, 1279 (Fed. Cir. 2010)). In other words, requiring the "amounts" to be "clinically proven effective" did not further define the express 2.5 and 75-100 mg "amounts" claimed in the remainder of the method.

Bayer explicitly distinguished another Federal Circuit case, *Allergan Sales, LLC v. Sandoz, Inc.*, 935 F.3d 1370 (Fed. Cir. 2019), which attributed patentable weight to claim limitations requiring particular safety and efficacy benchmarks in the context of a method of treatment claim. More specifically, the *Allergan* court held that two disputed "wherein" clauses were material to patentability because they "were functional limitations that limited the open-ended universe" of potential treatments "by specifying safety and efficacy benchmarks the overall composition must meet." *Bayer*, 2025 WL 2698408, at *3. The claim at issue in *Allergan* is reproduced below with the two functional "wherein" limitations highlighted in yellow and blue, respectively.

> **1.** A method of treating a patient with glaucoma or ocular hypertension comprising topically administering twice daily to an affected eye a single composition comprising 0.2% w/v brimonidine tartrate and 0.68% w/v timolol maleate, ***wherein*** the method is as effective as the administration of 0.2% w/v brimonidine tartrate monotherapy three times per day and ***wherein*** the method reduces the incidence of one o[r] more adverse events selected from the group consisting of conjunctival hyperemia, oral dryness, eye pruritus, allergic conjunctivitis, foreign body sensation, conjunctival folliculosis, and somnolence when compared to the administration of 0.2% w/v brimonidine tartrate monotherapy three times daily.

935 F.3d at 1372-73 (emphasis added). Critically, these "wherein" clauses required particular functional effects that were not the necessary result of performing the preceding steps in the claim. *Id.* at 1377-79 (Prost, C.J., concurring). The *Bayer* court found that, in contrast, its "clinically proven effective" term "serve[d] no analogous function in the claims at issue," which "already specify the exact dosage of [drugs] to be administered to a patient." 2025 WL 2698408, at *3.

The Federal Circuit used similar reasoning in *L'Oréal USA, Inc. v. Olaplex, Inc.*, 844 F. App'x 308, 324 (Fed. Cir. 2021), which UTC discussed in its post-trial briefing, and which also relied on *Allergan*. D.I. 431 at 4. *L'Oréal* analyzed a single independent claim directed to methods of bleaching hair and dependent claims with functional limitations requiring specific decreases in hair breakage. 844 F. App'x at 312. The court held that the dependent claims were entitled to patentable weight because they "state specific requirements rather than a general purpose or aspirational result for the claimed method." *Id.* at 324 (quoting *Allergan*, 935 F.3d at 1379).

II. Unlike the *Bayer* claims, the '327 patent's dependent claims functionally modify the broader method of independent claim 1.

The functional limitations recited in claims 5, 6, 9, and 17 of the '327 patent are fundamentally different from the "clinically proven effective" language that was found to lack patentable weight in *Bayer*. These claims impose specific safety and efficacy requirements that further define the claimed method of treatment, meaningfully limiting the open-ended universe of potential methods allowed by claim 1. They are therefore entitled to patentable weight like the claims in *Allergan* and *L'Oréal*.

A. The '327 patent claims are different than the *Bayer* claims.

The claims of the '327 patent are unlike those in *Bayer* for several reasons. First, claims 5, 6, 9, and 17 are entire dependent claims, not a redundant three-word phrase in an independent claim. Nothing in *Bayer* justifies reading as superfluous four dependent claims that the USPTO reviewed, allowed, and issued, and are thus presumed to have meaning. Each of claims 5, 6, 9, and 17 modifies the method of claim 1 by requiring that specific safety and/or efficacy benchmarks be achieved. No phrase in any of the dependent claims merely *describes* a method recited elsewhere, as was the case in *Bayer*. *See* 2025 WL 2698408, at *3 ("Because the claims of the '310 patent *already specify the exact dosages* . . . the additional limitation that the amounts be 'clinically proved effective' does not further define the dosages that are administered." (emphasis added)). Claims 5, 6, 9, and 17 contain no language analogous to the term in *Bayer*.

Instead, claims 5, 6, 9, and 17 align with those the court found to have patentable weight in *Allergan*. Like in *Allergan*, "Claim 1 is written in open format." *Allergan*, 935 F.3d at 1378; *see* '327 patent, 54:6-14 ("A method of improving exercise capacity in a patient . . . comprising . . . ."). Further, claim 1, which is broader than the dependent claims, requires "an effective amount of at least 15 micrograms up to a maximum tolerated dose" where that dose is administered by inhalation and with at least 6 micrograms per breath. This "effective amount" is explicitly defined as "an amount of compound that is *sufficient* to effect treatment" ('327 patent, 6:47-52 (emphasis added)), so altering variables, like formulation, device, and dose, within the claimed method of treatment impact the functional improvements the method yields and patients experience. *See infra* § II.B. Narrowing the open scope of claim 1, each dependent claim requires that the method of treatment cause quantifiable efficacy and safety improvements, *i.e.*, "specific benchmarks" that define the method falling within that narrowed dependent claim. *Allergan*, 935 F.3d at 1379 (Prost, C.J., concurring). Dependent claims 5, 6, 9, and 17 thus "limit[] the open-ended universe" of potential treatments "by specifying safety and efficacy benchmarks the overall [method] must meet," like in *Allergan*'s independent claim. *Bayer*, 2025 WL 2698408, at *3.

The intrinsic evidence confirms that dependent claims 5, 6, 9, and 17 functionally narrow claim 1. For example, the written description explains that the "effective amount will vary depending upon the patient" and "can be determined by titrating the dose upwards from a starting dose[.]" '327 patent, 6:52-59. The dependent claims thus functionally impact the dose to ensure that the method reaches "an amount" that is "*sufficient* to effect treatment." *Id.* at 6:47-52 (emphasis added). The written description is clear that the outcomes in the dependent claims impact the dose administered, explaining that clinicians "*adjusted the dose* on an individual patient

basis *to achieve* the maximum tolerated dose *leading to functional improvement*." *Id.* at 29:47-54 (emphasis added); *see also* PTX-0147.00003 (same).

B. The methods of claims 5, 6, 9, and 17 specifically narrow the method of claim 1.

The methods of claims 5, 6, 9, and 17 each require specific safety and efficacy benchmarks, and those methods are each only a subset of the methods within the broader scope of claim 1. Unlike in *Bayer* where the disputed term had no impact on the method, variations in, for example, dose, duration of administration, formulation, and inhalation device will impact the outcomes achieved, confirming that claims 5, 6, 9, and 17 have patentable weight.

Dose. Claim 1 recites doses between 15 micrograms and the patient's maximum tolerated dose. But the dose of treprostinil required to achieve the specific functional improvements required by claims 5, 6, 9, and 17 will not necessarily be the same as those that may provide *any* improvement in "exercise capacity" as required by claim 1. PTX-0147.00025 (patients whose maximum tolerated dose reached only 7-9 breaths experienced less functional improvement than patients whose maximum tolerated dose reached 10-12 breaths). Differences in dose also drive variations in response on variables like NT-proBNP. *Id.*; Tr. 669:25-672:15 (Dr. Hill admitting that not all patients would experience an NT-proBNP improvement as required by claim 5); *see also* PTX-0147.00008, 27; PTX-0395.00063-73; Tr. 823:1-825:6 (not all INCREASE patients experienced claimed benchmarks). Thus, unlike in *Bayer*, claim 1 of the '327 patent does *not* "already specify the exact dosages" that amount to the "additional limitation[s]" required by the dependent claims. *Bayer*, 2025 WL 2698408, at *3.

Duration of Administration. Claim 1 requires improving exercise capacity over any duration, while claims 5, 9, and 17 each require a method of treatment where the PH-ILD patient reaches certain other efficacy and safety benchmarks at specific time points. Claim 17, for example, requires a 10-meter improvement in six-minute walk distance after 8 weeks. Similarly, claims 5 and 9 require the recited improvements "after 8 weeks, 12 weeks, or 16 weeks[.]" The rate at which doses are titrated also may have an effect on the maximum tolerated dose achieved, meaning that the rate of dose titration also impacts functional outcomes. Tr. 818:25-819:10 ("We don't know what maximum dose [patients] would achieve if they started slower than the three breaths four times a day."). Further, the written description shows that improvements in exercise capacity in some patients could be achieved after just four weeks, thereby satisfying claim 1. '327 patent, figs. 4, 8; *see also* PTX-0147.00024, 29. A four-week administration, however, would not necessarily meet the requirements of claims 5, 9, and 17. Accordingly, there are methods of administration within the scope of claim 1 that are excluded by the specific functional benchmarks of the dependent claims.

Formulation and device. The evidence at trial made clear that meeting the functional requirements of these dependent claims can depend on the formulation and device used. D.I. 431 at 4. Dr. Nathan testified, unrebutted, that some formulations of inhaled treprostinil may not achieve the specific efficacy limitations of claims 5, 6, 9, and 17. Tr. 162:23-164:7 (discussing other formulations of inhaled treprostinil). Liquidia's method—using the Yutrepia formulation and device—will more likely than not satisfy the claims based on Liquidia's repeated representation that Yutrepia will perform "equivalent" to Tyvaso. D.I. 426 at 3-8; PTX-291.00005-06, 15. But other formulations that are not equivalent to Tyvaso and Yutrepia may not achieve the limitations

of claims 5, 6, 9, and 17 even though they would be within the scope of claim 1. Thus, the dependent claims functionally narrow the possible methods within the scope of claim 1.

As is clear, the dependent safety and efficacy limitations of claims 5, 6, 9, and 17 narrow the universe of potential treprostinil compositions and methods that may be used in claim 1. Any given method within claim 1 will therefore not necessarily provide the particular efficacy and safety benchmarks required by the dependent claims. This is the definition of patentable weight. *Allergan*, 935 F.3d at 1378-79; *L'Oréal*, 844 F. App'x at 324; *Bayer*, 2025 WL 2698408, at *3.

C. Claims 5, 6, 9, and 17 are controlled by *Allergan* and *L'Oréal*, not *Bayer*.

The efficacy and safety limitations of claims 5, 6, 9, and 17 of the '327 patent are analogous to those that the Federal Circuit found to have patentable weight in *Allergan*. 935 F.3d at 1372-73, 1379. There, the two disputed "wherein" limitations required that the method of treatment achieve equivalent efficacy and better safety as compared to another specified drug. 935 F.3d at 1378-79 (Prost, C.J., concurring); *L'Oréal*, 844 F. App'x at 324 (citing Chief Judge Prost's *Allergan* concurrence); *Bayer*, 2025 WL 2698408, at *3 (same). Those limitations meaningfully narrowed the claimed method because they "specify clear and measurable metrics" that must be met and are not "an inherent result" of the dosage limitations. *Allergan*, 935 F.3d at 1378-79.

As in *Allergan*, claims 5, 6, 9, and 17 of the '327 patent "state specific requirements rather than a general purpose or aspirational result for the claimed method." 935 F.3d at 1379. Each of these claims require improvements in particular benchmarks—*i.e.*, NT-proBNP, exacerbations of ILD, FVC, and six-minute walk distance—at particular timepoints. *See* D.I. 431 at 3-5. Thus, unlike *Bayer*, the functional limitations in claims 5, 6, 9, and 17 of the '327 patent further limit the open-ended scope of claim 1 "by specifying safety and efficacy benchmarks" that must be met in order to meet the narrower dependent claims. *Bayer*, 2025 WL 2698408, at *3. These claims instead much more closely resemble the dependent claims found to have patentable weight in *L'Oréal*, because they "limit the options covered by the subject matter defined by the claims on which they depend to options that produce the concretely specified results—thus making a difference in the manipulative steps." 844 F. App'x at 324.

Critically, Liquidia has failed to prove that the functional improvements required by claims 5, 6, 9, and 17 would be the inherent result of performing claim 1. *Id.*; *Allergan*, 935 F.3d at 1378-79. This is a further difference from *Bayer*, where the claimed method was "otherwise anticipated" and the limitation at issue was redundant to other limitations. 2025 WL 2698408, at *3. Here, claims 5, 6, 9, and 17 are not inherently anticipated—Liquidia instead relies on a flawed inherency position that this Court has called "close to frivolous." Tr. 635:14-16; *see* D.I. 424 at 1-2, 27-28. Just like the defendant in *Allergan*, Liquidia's "position fails for at least two reasons." 935 F.3d at 1380 (Prost, C.J., concurring). "First, [Liquidia] did not argue that the claims should be construed as being limited to [UTC]'s commercial embodiment [Tyvaso]." *Id.* "Second, there is no basis in the record before us for assuming that all formulations of the combination necessarily behave like [Tyvaso]." *Id.* In fact, the record evidence shows the opposite—not all formulations may behave like Tyvaso. Tr. 162:23-164:7. "Thus, [Liquidia]'s arguments based on the clinical trial data for [Tyvaso] carry little force." *Allergan*, 935 F.3d at 1380 (Prost, C.J., concurring).

Bayer, *Allergan*, and *L'Oréal* thus compel a finding that the functional safety and efficacy

limitations recited in claims 5, 6, 9, and 17 of the '327 patent are entitled to patentable weight.

III. Liquidia's argument regarding patentable weight is still forfeited.

Unlike in *Bayer* and *Allergan*, where a claim construction issue was timely raised, Liquidia forfeited its argument that claims 5, 6, 9, and 17 lack patentable weight. *See* D.I. 431 at 3. Liquidia never properly disclosed the theory in its invalidity contentions, never raised it during claim construction, and first raised patentable weight as an issue in a *Daubert* motion. *Id.* This defense is forfeited. D.I. 346; Tr. 978:4-979:8 ("But my question is: Isn't this a claim construction issue that should have been brought up long ago?"). Further, to the extent Liquidia now attempts to introduce new arguments based on *King* (which *Bayer* simply applies), those arguments were also forfeited. Liquidia committed substantial space in its post-trial briefing to patentable weight, but never cited *King* there. D.I. 424 at 1-3; D.I. 435 at 1. Because *Bayer* merely applies *King*—on which Liquidia could have relied—Liquidia has no basis to make new arguments now based on *Bayer*'s reiteration of prior caselaw. *See Kaufman v. Microsoft Corp.*, 34 F.4th 1360, 1369 (Fed. Cir. 2022).

IV. *Bayer* confirms that Liquidia's patentable weight theory is wrong.

Even if Liquidia had not forfeited its patentable weight argument, *Bayer* confirms that Liquidia's position is incorrect. Liquidia's discussion of patentable weight in its post-trial briefing was based primarily on a misreading of the infringement testimony of UTC's expert, Dr. Nathan, that was specifically directed to Yutrepia. D.I. 424 at 2-3. Contrary to Liquidia's suggestion, Dr. Nathan never testified that practicing claim 1 would *always and necessarily* produce the clinical benefits required by claims 5, 6, 9, and 17. D.I. 431 at 4; Tr. 162:16-164:7. Dr. Nathan instead testified that Yutrepia—which relies on UTC's INCREASE data *and* which Liquidia represents is equivalent to Tyvaso—would, more likely than not, infringe all asserted claims when administered according to its label. *Id.*; *see also* Tr. 95:19-96:25, 105:14-107:5, 117:17-19, 142:18-146:17. Again, when presented with the hypothetical of another drug company's product that did not rely on the INCREASE data and was not necessarily equivalent to Tyvaso, Dr. Nathan testified that he could not know whether that hypothetical product would infringe the claims. Tr. 162:23-164:7. Moreover, *Bayer* determined that three words in an *independent* claim lacked patentable weight but did not render "dependent claims as entirely a nullity," as Liquidia's arguments would here and as the Federal Circuit rejected in *L'Oréal*. 844 F. App'x at 324.

Liquidia also argued in its post-trial briefing that claims 5, 6, 9, and 17 lacked patentable weight because the claims did not recite "a comparison step." D.I. 424 at 3. Liquidia is wrong. Nothing in *Bayer* requires claims to recite a comparison step to warrant patentable weight; instead, limitations like these merit patentable weight where they "specify[] safety and efficacy benchmarks that the overall" claimed method "must meet." *Bayer*, 2025 WL 2698408, at *3; *see also Allergan*, 935 F.3d at 1378-79 (Prost, C.J., concurring). Claims 5, 6, 9, and 17 do that here. Accordingly, *Bayer* forecloses Liquidia's attempt to make "a comparison step" dispositive of patentable weight.

* * *

For the reasons set forth above, UTC respectfully requests that the Court find that claims 5, 6, 9, and 17 are entitled to patentable weight as required by *Bayer*, *Allergan*, and *L'Oréal*.

Respectfully submitted,

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cc: Clerk of Court (by hand delivery)
All Counsel of Record (by e-mail)